

**REMARKS**

The claims have been amended only for clarity. It will be noted that the claims no longer refer to direct complementarity between the SSRMs and the SARMs. It has also been clarified that the target is the mRNA transcribed from a gene to be silenced. It is believed that this makes the subject matter clearer.

In response to the Examiner's concern that double-stranded RNA is not specifically mentioned in the specification, applicants point out that the claims do not require that the SSRMs and SARMs be double-stranded. Of course, double-stranded forms are included within the scope of the claim.

Applicants note that the present specification itself states that double-stranded RNA is known to induce silencing in nematodes (see page 3, lines 10-26) and it concludes that there is a relationship between the SRMs of the invention and silencing in nematodes using double-stranded RNA (see page 11, line 34 – page 12, line 4 and page 12, lines 16-29).

Citation of the relationship between silencing effected by long double-stranded RNA in *C. elegans* and similar mechanisms in plants is further confirmed by the data obtained in the experiment set forth on page 24 of the specification. In this experiment, three tobacco lines carrying glucuronidase (GUS) transgenes were analyzed. Post-transcriptional gene silencing could be exhibited only in those lines where the gene was actually transcribed, and 25 nt GUS antisense RNA was detected only in the lines that underwent post-transcriptional gene suppression. The conclusion is that "25 nt antisense GUS RNA is dependent upon transcription from the 35S promoter." (page 24, lines 24-25). The transcription, of course, generates sense GUS RNA. As that is the case, the 25 nucleotide SARM must be polymerized using the transcribed sense GUS RNA as a template. Such polymerization requires that a double-stranded RNA be formed. Thus, one of skill in the art

would view the teaching of the specification to confirm that double-stranded RNA that includes the SARM was present during the post-transcriptional gene silencing process.

However, applicants again emphasize, that double-stranded SSRMs and SARMs are not specifically required by the claims.

Applicants further wish to comment on a rejection made earlier in the prosecution where double-stranded forms also were not required. This was a rejection for asserted lack of enablement based on the disclosure in Klahre, U., *et al.*, *PNAS* (2002) 99:1981-1986. This document demonstrates that, in plants, gene silencing can be effected by double-stranded RNA's that are short, but that single-stranded 21 nucleotide sense or 22 nucleotide antisense RNA's were unable to silence the relevant genes. Applicants point out that no experiment was done demonstrating that a combination of SSRMs and SARMs was or was not able to silence the relevant gene. Therefore, the Klahre paper simply does not describe an experiment that conforms to the requirements of the present claims.

Consideration of the amended claims is respectfully requested.

Applicants wish once again to thank Examiner Mehta for taking time to discuss this case with their representatives.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 616292000111.

Respectfully submitted,

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